

CLAIMS

What is claimed is:

- 5 1. A method for making an array, the method comprising:
 - (a) isolating a plurality of cellular polynucleotide sequences, whereby the sequences are isolated based on their accessibility in cellular chromatin; and
 - (b) attaching each of the isolated sequences to an address on a solid support.
- 10 2. An array comprising a plurality of accessible polynucleotide sequences, wherein:
 - (a) the sequences are isolated based on their accessibility in cellular chromatin; and
 - (b) each accessible sequence is located at a distinct address on a solid support.
- 15 3. The array of claim 2, wherein the accessible sequences are isolated from a plurality of different cell types from an organism.
4. The array of claim 2, wherein the accessible sequences are isolated from a single cell or tissue type from an organism.
- 20 5. The array of claim 2, wherein the accessible sequences are isolated according to the following procedure:
 - (a) isolating a first plurality of cellular polynucleotide sequences, whereby the sequences are isolated based on their accessibility in cellular chromatin from a first cell;
 - 25 (b) isolating a second plurality of cellular polynucleotide sequences, whereby the sequences are isolated based on their accessibility in cellular chromatin from a second cell;
 - (c) obtaining sequences that are unique to either the first or second plurality of cellular polynucleotide sequences; and
 - (d) attaching each of the isolated sequences obtained in step (c) to an address on a
 - 30 solid support.
6. A method of identifying a target sequence bound by a DNA-binding protein, the method comprising the steps of:

(a) contacting at least one DNA-binding protein with an array according to claim 2, under conditions such that the protein binds to accessible sequences comprising a target sequence bound by the protein;

(b) removing unbound proteins; and

5 (c) identifying the accessible sequences bound by the protein, thereby identifying target sequences for the protein.

7. A method of identifying a transcription factor, the method comprising the steps of:

10 (a) preparing a preparation of proteins from a cell;

(b) contacting the isolated proteins with an array according to claim 2, under conditions such that transcription factors in the protein preparation bind to accessible sequences comprising a target sequence bound by a transcription factor;

(c) removing unbound proteins; and

15 (d) identifying the proteins bound to the array.

8. A method for obtaining a regulatory profile of accessible sequences in a cell, the method comprising:

20 (a) isolating a plurality of polynucleotide sequences from the cell, whereby the sequences are isolated based on their accessibility in cellular chromatin;

(b) optionally amplifying the sequences obtained in step (a);

(c) optionally labeling the sequences of step (a) or (b);

(d) contacting the sequences of step (a), (b) or (c) with an array according to claim 3; and

25 (e) identifying the accessible sequences bound on the array, thereby identifying sequences that are accessible in the cell.

9. A method for identifying functional binding sites for a DNA-binding protein in a cell, the method comprising:

30 (a) subjecting a cell to conditions under which DNA-binding proteins are crosslinked to their binding sites in cellular chromatin;

(b) shearing the crosslinked cellular chromatin of step (a);

- (c) immunoprecipitating the sheared crosslinked chromatin of step (b) with an antibody which recognizes the DNA-binding protein;
- (d) reversing the crosslinks in the immunoprecipitate of step (c);
- (e) purifying the DNA from the immunoprecipitated material of step (d);
- 5 (f) optionally amplifying the DNA obtained in step (e);
- (g) optionally labeling the DNA of step (e) or (f);
- (h) contacting the DNA from step (e), (f) or (g) with an array according to claim 2;
- and
- (i) identifying the accessible sequences bound on the array, thereby identifying
- 10 functional binding sites for the DNA-binding protein in the cell.

10. A method of identifying a sequence in cellular chromatin, wherein the chromatin is covalently modified, the method comprising:

- (a) providing a sample of cellular chromatin;
- 15 (b) optionally subjecting the chromatin of step (a) to conditions under which DNA-binding proteins are crosslinked to their binding sites in cellular chromatin;
- (c) shearing the cellular chromatin of step (a) or (b);
- (d) immunoprecipitating the sheared chromatin of step (c) with an antibody which recognizes a covalent chromatin modification;
- 20 (e) purifying the DNA from the immunoprecipitated material of step (d);
- (f) optionally amplifying the DNA obtained in step (e);
- (g) optionally labeling the DNA of step (e) or (f);
- (h) contacting the DNA from step (e), (f) or (g) with an array according to claim 2;
- and
- 25 (i) identifying the accessible sequences bound on the array, thereby identifying sequences in cellular chromatin wherein the chromatin is covalently modified.

11. A method for characterizing the effects of a molecule on a cell, the method comprising:

- 30 (a) contacting the cell with the molecule;
- (b) isolating a first plurality of polynucleotide sequences from the cell of step (a), whereby the sequences are isolated based on their accessibility in cellular chromatin;
- (c) optionally amplifying the sequences obtained in step (b);

- (d) optionally labeling the sequences of step (b) or (c);
- (e) contacting the sequences of step (b), (c) or (d) with an array according to claim 2;
- and
- (f) identifying the accessible sequences bound on the array, thereby identifying
- 5 sequences that are accessible in the cell.

12. The method of claim 11, further comprising the steps of:
- (g) providing cells that have not been contacted with the molecule;
 - (h) isolating a second plurality of polynucleotide sequences from the cell of step (g),
 - 10 whereby the sequences are isolated based on their accessibility in cellular chromatin;
 - (i) optionally amplifying the sequences obtained in step (h);
 - (j) obtaining sequences that are unique to either the first or second plurality of polynucleotide sequences;
 - (k) optionally amplifying the sequences obtained in step (j);
 - 15 (l) optionally labeling the sequences of step (j) or (k);
 - (m) contacting the sequences of step (j), (k) or (l) with an array according to claim 2;
 - and
 - (n) identifying the accessible sequences bound on the array, thereby identifying differences in accessible sequences between cells that have and have not been contacted with
 - 20 the molecule.

13. A method of identifying single nucleotide polymorphisms (SNPs) in regulatory sequences of an individual, the method comprising the steps of:
- (a) preparing a library of regulatory DNA sequences from chromatin isolated from
 - 25 cells from the individual;
 - (b) optionally labeling the sequences of step (a);
 - (c) hybridizing the sequences of step (a) or (b) to an array according to claim 2 under stringent hybridization conditions, wherein the regulatory DNA sequences of the library hybridize to complementary accessible sequences on the array;
 - 30 (d) removing regulatory DNA sequences of the library that are not bound to accessible sequences on the array; and
 - (e) identifying accessible sequences on the array that are not hybridized to regulatory DNA sequences of the library, wherein the unbound accessible sequences on the array

suggest the presence of a SNP in regulatory sequences of the individual corresponding to the unbound accessible sequence.

5 14. A method for characterizing the effects of a stimulus on a cell, the method comprising:

- (a) subjecting the cell to the stimulus;
 - (b) isolating a first plurality of polynucleotide sequences from the cell of step (a), whereby the sequences are isolated based on their accessibility in cellular chromatin;
 - (c) optionally amplifying the sequences obtained in step (b);
 - 10 (d) optionally labeling the sequences of step (b) or (c);
 - (e) contacting the sequences of step (b), (c) or (d) with an array according to claim 2;
- and
- (f) identifying the accessible sequences bound on the array, thereby identifying sequences that are accessible in the cell.

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15. The method of claim 14, further comprising the steps of:

- (g) providing cells that have not been subjected to the stimulus;
 - (h) isolating a second plurality of polynucleotide sequences from the cell of step (g), whereby the sequences are isolated based on their accessibility in cellular chromatin;
 - 20 (i) optionally amplifying the sequences obtained in step (h);
 - (j) obtaining sequences that are unique to either the first or second plurality of polynucleotide sequences;
 - (k) optionally amplifying the sequences obtained in step (j);
 - (l) optionally labeling the sequences of step (j) or (k);
 - 25 (m) contacting the sequences of step (j), (k) or (l) with an array according to claim 2;
- and
- (n) identifying the accessible sequences bound on the array, thereby identifying differences in accessible sequences between cells that have and have not been subjected to the stimulus.

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